Clinical Policy: Mitoxantrone

Reference Number: CP.PHAR.258
Effective Date: 08/16
Last Review Date: 08/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for mitoxantrone.

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that mitoxantrone is **medically necessary** for the following indications:

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all):

1. Diagnosis of relapsing-remitting or secondary-progressive multiple sclerosis (MS);
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. If member has relapsing-remitting MS, failure of one of the following (a or b) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:
   a. Tecfidera or Gilenya and any of the following: an interferon-beta agent *(Avonex and Plegridy are preferred agents)*, or glatiramer *(Glatopa 20 mg and Copaxone 40 mg are preferred agents)*;
   b. Tecfidera and Gilenya;
5. Member will not use other disease modifying therapies for MS concurrently;
6. Member does not have baseline left ventricular ejection fraction < 50%;
7. Dose does not exceed 12 mg/m^2 every 3 months (total cumulative lifetime dose of 140 mg/m^2).

Approval duration: 3 months (1 dose)

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy

II. Continued Approval

A. Multiple Sclerosis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy (e.g., improved or maintained disease control evidenced by decreased or stabilized Expanded Disability Status Scale score or reduction in relapses or magnetic resonance imaging lesions);
3. Member is not using other disease modifying therapies for MS concurrently;
4. If request is for a dose increase, new dose does not exceed 12 mg/m^2 every 3 months (total cumulative lifetime dose of 140 mg/m^2).

Approval duration: 3 months (1 dose)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Mitoxantrone, a DNA-reactive agent that intercalates into DNA through hydrogen bonding, causes crosslinks and strand breaks. Mitoxantrone also interferes with RNA and is a potent inhibitor of topoisomerase II, an enzyme responsible for uncoiling and repairing damaged DNA. It has a cytocidal effect on both proliferating and nonproliferating cultured human cells, suggesting lack of cell cycle phase specificity. Mitoxantrone injection has been shown in vitro to inhibit B cell, T cell, and macrophage proliferation and impair antigen presentation, as well as the secretion of interferon gamma, TNFα, and IL-2.

Formulations:

Mitoxantrone is a sterile aqueous solution containing mitoxantrone hydrochloride at a concentration equivalent to 2 mg mitoxantrone free base per mL supplied in vials for multidose use (10 mL, 12.5 mL, and 15 mL).

FDA Approved Indication(s):

Mitoxantrone is an anthracenedione/intravenous infusion indicated for:

- Reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (i.e., patients whose neurologic status is significantly abnormal between relapses).
- Initial chemotherapy in combination with corticosteroids for the treatment of patients with pain related to advanced hormone-refractory prostate cancer.
- Initial therapy in combination with other approved drug(s) for the treatment of acute nonlymphocytic leukemia in adults, including myelogenous, promyelocytic, monocytic, and erythroid acute leukemias.

Limitations of use:

- Mitoxantrone is not indicated in the treatment of patients with primary progressive multiple sclerosis.

Appendices

Appendix A: Abbreviation Key

DNA: deoxyribonucleic acid
FDA: Food and Drug Administration
MS: multiple sclerosis
RNA: ribonucleic acid

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9293	Injection, mitoxantrone HCl, per 5 mg

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.18 MS Treatments. Criteria: clarified monotherapy restriction, added criteria for re-authorization. Requirement for the trial and failure of at least 2 preferred regimens from different classes added. Removed specific strength requirement from glatiramer.	06/16	08/16
Added age requirement. Removed MRI requirement. Updated preferencing to require at least one of the highly effective DMTs on formulary (Tecfidera or Gilenya). Removed hepatic impairment and hypersensitivity contraindications. Removed reasons to discontinue.	06/17	08/17

References

1. Mitoxantrone Prescribing Information. Irvine, CA: Teva Parenteral Medicines, Inc.; June 2012. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4d0f0f1a-31af-40fa-9c64-e90891fa6ce4. Accessed June 14, 2017.
2. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis: Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*. 2002; 58(2): 169-178.
3. Olek MJ. Diagnosis of multiple sclerosis in adults. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.UpToDate.com. Accessed June 13, 2017.
4. Costello K, Halper J, Kalb R, Skutnik L, Rapp R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. July 2016. Accessed June 13, 2017.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.